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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,897	10/25/2001	Manfred Eigen	EIGEN ET AL (DIV)	8308

7590 12/04/2002

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	10

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/032,897	Applicant(s) Eigen et al.
	Examiner Joyce Tung	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 17, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *47-72* is/are pending in the application.

4a) Of the above, claim(s) *69* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *47-68 and 70-72* is/are rejected.

7) ☒ Claim(s) *61 and 72* is/are objected to.

8) ☒ Claims *47-72* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 47-68 and 70-72 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that Group I and Group II should be examined together because any search for the group embodied in claims 47-68 and 70-72 would necessarily include a search for the group embodied in claim 69. This is not found persuasive because Group I, claims 47-69 and 70-72 are drawn to a process for destabilizing a viral quasi-species-distribution without inducing resistance to therapeutic agents by replication of nucleic aid of viruses present in the quasi-species-distribution, while Group II, claim 69 is drawn to a method for the treatment of disease caused by a virus comprising inducing a rate of misincorporation during viral replication higher than the rate of misincorporation of the wild-type virus. Thus, based upon the different methods as discussed above, they lack the same or corresponding special technical features.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should

appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(I) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

Drawings

3. There are no brief descriptions for figs 5 and 6 in the specification.

Claim Objections

4. Claims 61 and 72 are objected to because of the following informalities: the phrase "a higher error rate of rate of misincorporation" might have typographic error. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the infected target cell with AZT or Acyclovir (See pg. 1 of the specification), does not reasonably provide enablement for treating the affected target cells with any substances as claimed in claim 61. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to carry out or make the invention commensurate in scope with these claims.

In Exparte Forman,230 USPQ 546 (Bd. App. 1986), the Board considered the issue of enablement in molecular biology. The Board summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering these factors: (a) in order to practice the invention, the practitioner must be able to apply any substances to the affected target cells, (b) the specification provides guidance only with regard to treat the affected cells with AZT or Acyclovir (See pg. 1 of the specification); (c) in the specification there is really no specific wording example to treat the affected target cells with any substances; (d) the invention is directed to treat the affected target cells with any substances; (e)

the prior art, USPatent no. 4,536,398 teaches a substance SF-2140 to treat viral diseases (See Abstract); (f) the level of skill in molecular biology is high; (g) the claims are broadly drawn, reciting treating viral diseases with any substances. Based on the above analysis, one of ordinary kill in the art would be subject to undue experimentation in applying any substances to treat viral diseases.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 47-68 and 70-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 47-60, 62-68 and 70-72 are vague and indefinite because no active steps are recited which define the process. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion. See Ex parte Erlich, 3 USPQ2d, p. 1011 (Bd. Pat. App. Int. 1986).

b. Claims 47-60, 62-68 and 70-72 are vague and indefinite because the language "the viral wild-type replication system" in claim 47 has no antecedent basis.

c. Claim 52 is vague and indefinite because of the language "the target cells" and "the respective stable quasi-species-distribution" which has no antecedent basis.

d. Claim 53 is vague and indefinite because of the language "the replication system RNA or DNA" which has no antecedent basis. Since in claim 47, there are phrases " a defective replication system" and "the viral wild-type replication system", it is unclear which phrase is referred to. Clarification is required.

e. Claim 54 is vague and indefinite because of the language "the gene therapy" which has no antecedent basis.

f. Claim 55 is vague and indefinite because of the language "superinfection of the target cell". It is unclear what is the definition of "superinfection" compared with infection.

g. Claim 60 is vague and indefinite because of the language "a characteristic superiority parameter s". It is unclear how the language is defined in the specification. And the language "the respective virus genome", "the other replicatable nucleic acid" and "the not infected target cell" have no antecedent basis. In addition, the phrase " a combination of the replication system" is unclear which replication system is involved in the combination since there are a lot of replication system, for example, a defective replication system, or the replication system of the wild-type virus. Clarification is required.

h. Claims 61 and 72 are vague and indefinite because of the language "the affected target cells" and "the target cells" which have no antecedent basis.

I. Claim 64 is vague and indefinite because the phrase "the native replication system" has no antecedent basis.

7. The references "The fifth Paul Ehrlich Lecture virus strains as models of molecular evolution" (Presented by Dr. Manfred Eigen on March 6, 1992, at the National Institute of Health, Bethesda, MD, USA), "Viral Quasispecies" (Eigen, Scientific American, 1993, Vol. 269, (1), pg. 32-39), "Foot and mouth disease virus populations are quasispecies" (Domingo et al. Current topics in microbiology and immunology, Vol. 176, 1992, pg. 32-47), "Fidelity of HIV-1 reverse transcriptase" (Preston et al. Science, 1988, Vol. 242, pg. 1168-1171), "Sequence space and quasispecies distribution" (Eigen et al. RNA Genetics, 1988, Vol. 3, Chapter 2) were reviewed. The reference "The fifth Paul Ehrlich Lecture virus strains as models of molecular evolution" teaches what is viral quasispecies (See pg. 392). The reference, "Viral Quasispecies" also teaches what is viral quasispecies (see pg. 35). The reference "Foot and mouth disease virus populations are quasispecies" teaches the foot and mouth disease virus. The reference "Fidelity of HIV-1 reverse transcriptase" teaches that the specificity of misincorporation may provide a basis for the systematic construction of antiviral nucleotide" (See the Abstract). The reference "Sequence space and quasispecies distribution" teaches that population of RNA viruses are of a quasispecies nature which has mutation rates (See pg. 230-231). These references fail to provide teachings or suggestion to the limitations of instant invention that is a process for destabilizing a viral quasi-species-distribution without inducing resistance to therapeutic agents by replication of nucleic acid of viruses present in the quasi-species-distribution by means of a defective replication system.

8. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

November 28, 2002

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
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